REMARKS

Claims 1-72 are pending in this application. Claims 38-45 are allowed. Claims 1-36 and 46-72 stand rejected. Claim 37 stands objected.

1. Claim Rejections – 35 U.S.C. § 112, first paragraph

Claims 68, 69, 71 and 72 stand rejected under 35 U.S.C. § 112, first paragraph for allegedly lacking enablement. Applicants respectfully traverse.

The Office Action alleges that the specification, while enabling for epilepsy, does not enable the prevention of seizures or depressing the central nervous system. Oxcarbazepine is currently marketed as TRILEPTAL® for the treatment of epilepsy. The Physician's Desk Reference (PDR) teaches the clinical pharmacology of oxcarbazepine as follows:

> In vitro electrophysiological studies indicate that [oxcarbazepine and its metabolite] produce blockade of voltage-sensitive sodium channels, resulting in stabilization of hyperexcited neural membranes, inhibition of repetitive neuronal firing, and diminution of propagation of synaptic impulses. These actions are thought to be important in the prevention of seizure spread in the intact brain. In addition, increased potassium conductance and modulation of high-voltage activated calcium channels may contribute to the anticonvulsant effects of the drug.

Physician's Desk Reference, 59 ed., 2005, p. 2380. Oxcarbazepine and its active metabolite exhibit anticonvulsant properties in patients. *Id.* The oxcarbazepine of the invention, when absorbed in blood, produces the same pharmacological effect as oxcarbazepine marketed under TRILEPTAL®. Therefore, claims 68 and 69 directed to the prevention or reduction of seizures are fully enabled. Similarly, it is commonly known in the field that drugs for the treatment of seizures, i.e. oxcarbazepine, are central-nervous system depressants. Therefore, claims 71 and 72 are also enabled by the specification.

One of the factors to consider for enablement is the level of one of ordinary skill in the art. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). As illustrated by the PDR, the level of skill in the field of treating epilepsy with oxcarbazepine is sufficiently high. The Office Action alleges that no screening protocols or working examples are provided. The PDR discloses numerous clinical studies performed to determine the effectiveness of oxcarbazepine. Four randomized, double-blind, multicenter trials were performed to demonstrate the efficacy of oxcarbazepine as monotherapy. *Physician's Desk Reference*, p. 2381, col. 2. In addition, the effectiveness of oxcarbazepine as an adjunctive therapy for

partial seizures was established in two multicenter, randomized, double-blind placebo-controlled trials. *Physician's Desk Reference*, p. 2381, col. 3. Based on the vast background information and instruction from the PDR, one of ordinary skill in the art would know how oxcarbazepine may be used to treat epilepsy. Therefore, claims 68, 69, 71 and 72 are fully enabled by the specification.

2. Claim Rejections – 35 U.S.C. § 112, second paragraph

Claims 1-32, 34-36, and 46-72 stand rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite for failing to particularly point out and distinctively claim the subject matter regarded as the invention. Applicants respectfully traverse.

a) The Office Action alleges that claims 1, 5-11 and 58-72 are indefinite in that it is not known what is meant by "oxcarbazepine Form B." Claim 1 has been cancelled, and applicant wishes to pursue claims identifying the oxcarbazepine form by its PXRD pattern which encompass the same or broader scope than the cancelled claim. The currently amended claims recite the oxcarbazepine form by its PXRD pattern.

b) The Office Action alleges that claims 2-4 are indefinite in that it is not known what is meant by oxcarbazepine having the disclosed PXRD pattern. Identifying crystal forms by their PXRD peaks is a very common practice in the art. "The existence of polymorphs is best established by x-ray crystallographic examination." Byrn, S.R. *Solid-State Chemistry of Drugs*, p. 79 (Academic Press 1982).

> X-ray powder diffraction is perhaps the "gold standard" for the qualitative determination of crystallinity. Not only can the presence of a crystalline phase by confirmed, but since each polymorph produces a unique diffraction pattern, the question of which polymorph crystallized can be addressed.

Brittain, H.G., *Polymorphism in Pharmaceutical Solids* p. 398-99 (Marcel Dekkler 1999). Many patents have issued from the USPTO on polymorphs claimed by their PXRD patterns, such as U.S. Pat. Nos. 6,294,686; 6,365,574; 6,452,054; 6,465,496; 6,500,987; 6,599,884; 6,605,636; 6,610,718; 6,696,601; 6,710,184; 6,767,913; 6,734,314; 6,677,373; 6,683,106; 6,696,479; 6,713,481; 6,720,453; 6,723,728; 6,762,299; and 6,800,635. Furthermore, the term "crystalline" has been added to the claims to clarify that the oxcarbazepine forms have particular crystal structures. Applicants therefore respectfully submit that the currently amended claims are sufficiently definite to distinguish the invention.

c) The same rejection as in section a) is raised for claims 12, 16-20, 52 and 58-72, which are directed to oxcarbazepine Form C. Claim 12 has been cancelled, and applicant wishes to pursue claims identifying the oxcarbazepine form by its PXRD pattern which encompass the same or broader scope than the cancelled claim. For the same reasons stated above, the currently amended claims are sufficiently definite to distinguish the invention.

d) The same rejection as in section b) is raised for claims 13-15. For the same reasons stated above, the currently amended claims are sufficiently definite to distinguish the invention.

e) Claim 13 has been amended to include a period indicating the end of the claim.

f) The same rejection as in section a) is raised for claims 21, 24-32 and 58-72, which are directed to oxcarbazepine Form D. Claim 21 has been cancelled, and applicant wishes to pursue claims identifying the oxcarbazepine form by its PXRD pattern which encompass the same or broader scope than the cancelled claim. For the same reasons stated above, the currently amended claims are sufficiently definite to distinguish the invention.

g) The same rejection as in section b) is raised for claims 22-23. For the same reasons stated above, the currently amended claims are sufficiently definite to distinguish the invention.

h) The same rejection as in section a) is raised for claim 34, which is directed to oxcarbazepine chloroform solvate Form E. Claim 34 has been cancelled, and applicant wishes to pursue claims identifying the oxcarbazepine form by its PXRD pattern which encompass the same or broader scope than the cancelled claim.

i) The same rejection as in section b) is raised for claims 35-36. For the same reasons discussed above, the currently amended claims are sufficiently definite to distinguish the invention.

j) The same rejection as in section a) is raised for claims 46-51 and 53-57, which recite oxcarbazepine Form A. The currently amended claims recite the oxcarbazepine form by its PXRD pattern and are now sufficiently definite to distinguish the invention for the same reasons stated above.

k) The same rejection as in section a) is raised for claims 58-72 , which recite oxcarbazepine Form E. The currently amended claims recite the oxcarbazepine form by its

PXRD pattern and are now sufficiently definite to distinguish the invention for the same reasons stated above.

3. Claim Rejections – 35 U.S.C. § 102

Claims 1, 12, 21, 58-64, 68-69 and 71 stand rejected under 35 U.S.C. § 102 (b) as allegedly being anticipated by Schindler, U.S. Patent No. 3,716,640. Applicants respectfully traverse.

The Office Action alleges that a polymorph is a specific crystal form of a compound, but a pharmaceutical composition of a polymorphic form as a non-solid no longer possesses its crystalline properties. Claims 1, 12, and 21 have been cancelled. The rejection is now moot.

Claims 58-64, 68-69 and 71 encompass pharmaceutical compositions comprising oxcarbazepine forms of the invention. Pharmaceutical compositions of the invention comprise the oxcarbazepine polymorphs in solid form where their crystalline structures are retained. For example, compositions in tablet, powder, gel, capsule or suspension forms contain polymorphs as solids.

Even if polymorphic forms may be lost when absorbed into the blood, the pending claims are not directed to oxcarbazepine in blood but instead to oxcarbazepine in a pharmaceutical composition prior to absorption. The *Schering v. Geneva* decision provides guidance for this case. In *Schering*, the metabolite of a known active ingredient was found to be inherently anticipated by the administration of the active ingredient because the metabolite necessarily and inevitably formed in the human body. *See Schering Corp. v. Geneva Pharms., Inc.*, 339 F.3d 1373 (Fed. Cir. 2003). However, the court expressly distinguished a claim to a metabolite per se, which would encompass the metabolite when absorbed in blood, from a claim to a pharmaceutical composition containing the metabolite before administration:

> A skilled patent drafter, however, might fashion a claim to cover the metabolite in a way that avoids anticipation. For example, the metabolite may be claimed in its pure and isolated form, as in Kratz and Bergstrom, or as a pharmaceutical composition (e.g., with a pharmaceutically acceptable carrier). The patent drafter could also claim a method of administering the metabolite or the corresponding pharmaceutical composition. The '233 patent would not provide an enabling

> disclosure to anticipate such claims because, for instance, the '233 patent does not disclose isolation of DCL.

Id. at 1381. The patent in *Schering* contained claims directed to pharmaceutical compositions and methods of treating allergic reactions by administering compounds that include the metabolite. *See id.* These claims were not found to be anticipated by the reference '233 patent even though the reference anticipated the metabolite after administration of the drug. *Id.* By analogy, the pending claims are not anticipated because they are not directed to oxcarbazepine absorbed in blood, but to pharmaceutical compositions comprising the polymorphs prior to administration. The Schindler patent does not disclose the particular oxcarbazepine crystalline forms of the invention, nor does it disclose pharmaceutical compositions comprising them. Therefore, claims 58-64, 68-69 and 71 cannot be anticipated by Schindler.

Claims 1, 12, 21, 58-64, 68-69 and 71 also stand rejected under 35 U.S.C. § 102 (b) as allegedly being anticipated by Boireau et al., U.S. Patent No. 5,658,900. Applicants respectfully traverse.

For the same reasons discussed above, claims 1, 12, 21, 58-64, 68-69 and 71 are not anticipated by the Boireau patent, which discloses only a method of treating Parkinsonian syndrome using oxcarbazepine. The Boireau patent fails to state the type of oxcarbazepine polymorph used. The Boireau patent fails to disclose any process for preparing the oxcarbazepine polymorphs, nor does it provide any examples relating to such preparation. Boireau only cites to EP 50,589, which is published in German. Examples 1-3 in EP 50,589 seem to discuss only the preparation of pharmaceutical compositions, not the preparation of oxcarbazepine itself.

Claim 37 is objected to for being dependent upon a rejected base claim 33. As mentioned above, claim 33 is not anticipated by either the Schindler or Boireau patent. Therefore, the objection for claim 37 should be withdrawn.

If any outstanding issues remain, the examiner is invited to telephone the undersigned at the telephone number indicated below to discuss the same. No fee is believed to be due for the submission of this response. Should any fees be required, please charge such fees to Kenyon & Kenyon, LLP Deposit Account No. 11-0600.

Respectfully submitted,

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